

## Bone Density Following Three Years of Recovery from Long-Duration Space-Flight

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**Background:** Bone loss during long-duration space flight is well recognized, but the long-term implications on bone health following return from flight remain unclear. Among US crew who were involved in long-duration missions in space (Mir and ISS), we have previously shown that at ~12 months following return, men, but not women, had BMD values at most sites that were still lower than would be expected had they not been exposed to a prolonged period of microgravity. We now extend our observations to 3 years of follow-up post-flight.

**Methods:** Of 32 US crew who have been involved on long-duration space flights, 16 have had BMD measurements both immediately and at ~3 years post-flight, 2 of whom were women. We restricted analyses to men. We examined the observed changes in BMD (g/cm<sup>2</sup>) in the 14 male US crew, immediately and 3 years post-flight, relative to comparable age-expected changes derived from 348 men (age range: 22-90 years; 150 of whom were <50 years of age) representing an age-stratified, random sample of the adult community population. BMD measurements, using Hologic QDR 2000, were made at the total hip, lumbar spine, ultradistal and midshaft radius, and total body (sites also measured in US crew). Men were measured at baseline, 2, and 4 years. Linear mixed effects models were used to predict follow-up BMD using baseline BMD, age, and follow-up time, adjusting for the fact that most people were measured more than once. In US crew (14 men, mean  $\pm$  SD age: 47  $\pm$  5 years, range 37-54 years, at pre-flight scan), BMD was measured pre-flight, immediately after and at least 3 years post-flight using Hologic QDR 2000, QDR 4500 and Discovery scanners. The majority had pre- and post-flight BMD on similar machines. Immediate post-flight BMD was performed a median of x (range: x-xx) days after return, with a median flight duration of 161 (range: 115-196) days. The 3 year post-flight BMD were performed a median of 36 (range: x-x) months after return. None of the 14 male US crew had a second long-duration flight in the interim.

**Results:** Using their age, pre-flight BMD and follow-up time, post-flight BMD values for each US crew were predicted based on the model developed from the community sample. The predicted and observed BMD and rates of change immediately and 3 years post-flight for US crew are presented in the table. We found BMD measures to be either stable or improve by 3 years relative to their immediate post-flight BMD, however only total hip BMD still remains significantly lower than would be expected had they not been exposed to microgravity.

**Conclusion:** Among male US crew, who have had their BMD measured following at least 3 years of recovery post long-duration flight, they continue to have lower BMD at the hip than would be expected, raising potential concerns regarding future hip fracture risk.

BMD Site	Mean Immediate Post Flight BMD (% change/month)			Mean Three Year Post Flight BMD (% change/month)		
	Predicted	Observed	p-value	Predicted	Observed	p-value
Total Hip	1.063 (0.05)	0.994 (-0.76)	<0.001	1.066 (0.02)	1.047 (-0.03)	<0.001
Lumbar Spine	1.081 (0.11)	1.016 (-0.58)	<0.001	1.084 (0.03)	1.069 (-0.00)	0.11
Ultradistal Radius	0.558 (-0.05)	0.550 (-0.20)	0.12	0.541 (-0.08)	0.551 (-0.04)	0.005
Mid Shaft Radius	0.755 (0.19)	0.741 (-0.00)	0.03	0.749 (0.02)	0.741 (0.00)	0.28
Total Body	1.288 (-0.04)	1.262 (-0.26)	0.009	1.284 (-0.01)	1.261 (-0.05)	0.19